03-19-07

A27/615

PTO/SB/21 (09-06)
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Application Number	10/611,531
Filing Date	June 30, 2003
First Named Inventor	Subramanian S. Venkatraman
Art Unit	1615
Examiner Name	Ghali, Isis A D
Attorney Docket Number	ARC 2869 N1

ENCLOSURES *(Check all that apply)*

- ☐ Fee Transmittal Form
  - ☐ Fee Attached
- ☐ Amendment/Reply
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  - ☐ Affidavits/declaration(s)
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- ☐ Information Disclosure Statement
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- ☐ Reply to Missing Parts/ Incomplete Application
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- ☐ Petition
- ☐ Petition to Convert to a Provisional Application
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1. Return Receipt Postcard
2. Transmittal (1 pg.)
3. Appellant's Breif (38 pp.)
4. Fee Sheet (1 pg.)

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	ALZA Corporation		
Signature	Philip Yip		
Printed name	Philip Yip		
Date	3-15-2007	Reg. No.	37,265

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FEE TRANSMITTAL For FY 2007

MAR 15 2007

☐ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT	($)	500.00

Complete if Known	
Application Number	10/611,531
Filing Date	June 30, 2003
First Named Inventor	Subramanian S. Venkatraman
Examiner Name	Ghali, Isis A D
Art Unit	1615
Attorney Docket No.	ARC 2869 N1

METHOD OF PAYMENT (check all that apply)

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☒ Deposit Account Deposit Account Number: 10-0750 Deposit Account Name: Johnson & Johnson

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1. BASIC FILING, SEARCH, AND EXAMINATION FEES

	FILING FEES		SEARCH FEES		EXAMINATION FEES		
		Small Entity		Small Entity		Small Entity	
Application Type	Fee ($)	Fee ($)	Fee ($)	Fee ($)	Fee ($)	Fee ($)	Fees Paid ($)
Utility	300	150	500	250	200	100	
Design	200	100	100	50	130	65	
Plant	200	100	300	150	160	80	
Reissue	300	150	500	250	600	300	
Provisional	200	100	0	0	0	0	

2. EXCESS CLAIM FEES

Fee Description	Fee ($)	Small Entity Fee ($)
Each claim over 20 (including Reissues)	50	25
Each independent claim over 3 (including Reissues)	200	100
Multiple dependent claims	360	180

Total Claims	Extra Claims	Fee ($)	Fee Paid ($)
_____ - 20 or HP =	_____ x	_____ =	_____

HP = highest number of total claims paid for, if greater than 20.

Indep. Claims	Extra Claims	Fee ($)	Fee Paid ($)
_____ - 3 or HP =	_____ x	_____ =	_____

HP = highest number of independent claims paid for, if greater than 3.

Multiple Dependent Claims	
Fee ($)	Fee Paid ($)
_____	_____

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper (excluding electronically filed sequence or computer listings under 37 CFR 1.52(e)), the application size fee due is $250 ($125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

Total Sheets	Extra Sheets	Number of each additional 50 or fraction thereof	Fee ($)	Fee Paid ($)
_____ - 100 =	_____ / 50 =	_____ (round **up** to a whole number) x	250.00 =	0.00

4. OTHER FEE(S)

	Fees Paid ($)
Non-English Specification, $130 fee (no small entity discount)	
Other (e.g., late filing surcharge): Appellant's Brief	500.00

SUBMITTED BY

Signature		Registration No. (Attorney/Agent) 37,265	Telephone 650-564-2024
Name (Print/Type)	Philip Yip		Date March 15, 2007

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: ALZA Corporation Inventor(s): Venkatrman et al. Application No.: 10/611,531 Filed: June 30, 2003 Title: TRANSDERMAL DRUG DELIVERY DEVICES COMPRISING A POLYURETHANE DRUG RESERVOIR	Group Art Unit: 1615 Examiner: Ghali, Isis A D **Attorney Docket No.:** ARC 2869 N1

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Alexandria, VA 22313-1450

APPELLANT'S BRIEF

03/19/2007 FMETEKI1 00000064 100750 10611531
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Real Party in Interest

The real party in interest in this proceeding is ALZA Corporation, the Assignee of record, a wholly owned subsidiary of Johnson & Johnson.

Related Appeals and Interferences

Neither Appellant nor its agents are aware of any prior or pending appeals, judicial proceedings or interferences which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

Status of Claims

Claims 1-11, 34-53, 58 and 61 were canceled. Claims 12-33 and 54-57, and 59-60 stand finally rejected under 35 U.S.C. § 102 (a) or 103(a) and are appealed. A copy of the claims on appeal are in the Claims Appendix of this Brief.

Status of Amendments

An amendment after the Final Rejection mailed on October 20, 2006 was submitted on December 19, 2006 and was entered. No subsequent amendment was filed thereafter.

Summary of Claimed Subject Matter

Claim 12 is directed to a transdermal drug delivery device having a backing layer, a drug reservoir and a means for maintaining the device in drug transmitting relationship with a body surface or membrane. The drug reservoir is on or adjacent the skin-proximal side of the backing layer. The drug reservoir has a melt-blended mixture of at least one drug and a polymer consisting of polyurethane polymer. The polyurethane polymer has a process temperature of less than about 150 °C. The polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in the drug reservoir. (Page 8, line 1 to 21; page 18, line 18 to page 19, line 4; page 22, FIGs. 1-3)[1].

Claim 13 is directed to a transdermal drug delivery device having a backing layer, a drug reservoir and a means for maintaining the device in drug transmitting relationship with a body surface or membrane. The drug reservoir is on or adjacent the skin-proximal side of the backing layer. The drug reservoir has a melt-blended mixture of at least one

[1] Page and paragraph designations refer to those found in the originally filed specification.

drug and a polymer consisting of polyurethane polymer. The polyurethane polymer has a process temperature of less than about 150 °C. The polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in the drug reservoir. The polyurethane polymer has a process temperature of less than about 100 °C. (Page 8, line 1 to 21; page 18, line 18 to page 19, line 4; page 22; FIGs. 1-3)

Claim 14 is directed to a transdermal drug delivery device having a backing layer, a drug reservoir and a means for maintaining the device in drug transmitting relationship with a body surface or membrane. The drug reservoir is on or adjacent the skin-proximal side of the backing layer. The drug reservoir has a melt-blended mixture of at least one drug and a polymer consisting of polyurethane polymer. The polyurethane polymer has a process temperature of less than about 150 °C. The polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in the drug reservoir. The polyurethane polymer has a process temperature of 40 – 90 °C. (Page 8, line 1 to 21; page 18, line 18 to page 19, line 4; page 22; FIGs. 1-3)

Claim 15 is directed to a transdermal drug delivery device having a backing layer, a drug reservoir and a means for maintaining the device in drug transmitting relationship with a body surface or membrane. The drug reservoir is on or adjacent the skin-proximal side of the backing layer. The drug reservoir has a melt-blended mixture of at least one drug and a polymer consisting of polyurethane polymer. The polyurethane polymer has a process temperature of less than about 150 °C. The polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in the drug reservoir. The polyurethane polymer polyurethane polymer is a polyether polyurethane. (Page 8, line 1 to 21; page 22; page 16, lines 3 to 13; FIGs. 1-3)

Claim 16 is directed to a transdermal drug delivery device having a backing layer, a drug reservoir and a means for maintaining the device in drug transmitting relationship with a body surface or membrane. The drug reservoir is on or adjacent the skin-proximal side of the backing layer. The drug reservoir has a melt-blended mixture of at least one drug and a polymer consisting of polyurethane polymer. The polyurethane polymer has a process temperature of less than about 150 °C. The polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in

the drug reservoir. The polyurethane polymer comprises the reaction product of at least one aliphatic diisocyanate, at least one high molecular weight polyether polyol, and at least one low molecular weight glycol. (Page 8, line 1 to 21; page 23; page 16, lines 3-13 FIGs. 1-3)

Claim 17 is directed to a transdermal drug delivery device having a backing layer, a drug reservoir and a means for maintaining the device in drug transmitting relationship with a body surface or membrane. The drug reservoir is on or adjacent the skin-proximal side of the backing layer. The drug reservoir has a melt-blended mixture of at least one drug and a polymer consisting of polyurethane polymer. The polyurethane polymer has a process temperature of less than about 150 °C. The polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in the drug reservoir. The polyurethane polymer comprises the reaction product of at least one aliphatic diisocyanate, at least one high molecular weight polyether polyol, and at least one low molecular weight glycol. The diisocyanate comprises methylene bis(cyclohexyl) diisocyanate, the polyether polyol is selected from the group consisting of poly tetramethylene glycol, poly propylene glycol, and polyethylene glycol. (Page 8, line 1 to 21; page 23; page 16, lines 3-13; FIGs. 1-3)

Claim 18 is directed to a transdermal drug delivery device having a backing layer, a drug reservoir and a means for maintaining the device in drug transmitting relationship with a body surface or membrane. The drug reservoir is on or adjacent the skin-proximal side of the backing layer. The drug reservoir has a melt-blended mixture of at least one drug and a polymer consisting of polyurethane polymer. The polyurethane polymer has a process temperature of less than about 150 °C. The polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in the drug reservoir. The polyurethane polymer comprises the reaction product of at least one aliphatic diisocyanate, at least one high molecular weight polyether polyol, and at least one low molecular weight glycol. The diisocyanate comprises methylene bis(cyclohexyl) diisocyanate, the polyether polyol is selected from the group consisting of poly tetramethylene glycol, poly propylene glycol, and polyethylene glycol. The low molecular weight glycol is 1,4-butane diol. (Page 8, line 1 to 21; page 23; page 16, lines 3-13; FIGs. 1-3)

Claim 19 is directed to a transdermal drug delivery device having a backing layer, a drug reservoir and a means for maintaining the device in drug transmitting relationship with a body surface or membrane. The drug reservoir is on or adjacent the skin-proximal side of the backing layer. The drug reservoir has a melt-blended mixture of at least one drug and a polymer consisting of polyurethane polymer. The polyurethane polymer has a process temperature of less than about 150 °C. The polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in the drug reservoir. The polyurethane polymer comprises the reaction product of at least one aliphatic diisocyanate, at least one high molecular weight polyether polyol, and at least one low molecular weight glycol. The diisocyanate comprises methylene bis(cyclohexyl) diisocyanate, the polyether polyol is selected from the group consisting of poly tetramethylene glycol, poly propylene glycol, and polyethylene glycol. The polyether polyol is a mixture of at least two polymers selected from the group consisting of polytetramethylene ether glycol, polypropylene glycol, polyethylene glycol, and propylene glycol. (Page 8, line 1 to 21; page 23; page 16, lines 3-13; FIGs. 1-3)

Claim 20 is directed to a transdermal drug delivery device having a backing layer, a drug reservoir and a means for maintaining the device in drug transmitting relationship with a body surface or membrane. The drug reservoir is on or adjacent the skin-proximal side of the backing layer. The drug reservoir has a melt-blended mixture of at least one drug and a polymer consisting of polyurethane polymer. The polyurethane polymer has a process temperature of less than about 150 °C. The polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in the drug reservoir. The drug reservoir contains 0 - 20 wt% of at least one permeation enhancer. (Page 8, line 1 to 21; page 23; page 17, lines 5-6; FIGs. 1-3)

Claim 21 is directed to a transdermal drug delivery device having a backing layer, a drug reservoir and a means for maintaining the device in drug transmitting relationship with a body surface or membrane. The drug reservoir is on or adjacent the skin-proximal side of the backing layer. The drug reservoir has a melt-blended mixture of at least one drug and a polymer consisting of polyurethane polymer. The polyurethane polymer has a process temperature of less than about 150 °C. The polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in

the drug reservoir. The drug reservoir contains 0 - 20 wt% of at least one permeation enhancer. The permeation enhancer is selected from the group consisting of monoglucerides and lauryl pyroglutamate. (Page 8, line 1 to 21; page 23; page 18, lines 8-11; FIGs. 1-3)

Claim 22 is directed to a transdermal drug delivery device having a backing layer, a drug reservoir and a means for maintaining the device in drug transmitting relationship with a body surface or membrane. The drug reservoir is on or adjacent the skin-proximal side of the backing layer. The drug reservoir has a melt-blended mixture of at least one drug and a polymer consisting of polyurethane polymer. The polyurethane polymer has a process temperature of less than about 150 °C. The polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in the drug reservoir. The drug reservoir contains about 0.1 - 40 wt% of at least one drug. (Page 8, line 1 to 21; page 23; page 16, lines 15-18; FIGs. 1-3)

Claim 23 is directed to a transdermal drug delivery device having a backing layer, a drug reservoir and a means for maintaining the device in drug transmitting relationship with a body surface or membrane. The drug reservoir is on or adjacent the skin-proximal side of the backing layer. The drug reservoir has a melt-blended mixture of at least one drug and a polymer consisting of polyurethane polymer. The polyurethane polymer has a process temperature of less than about 150 °C. The polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in the drug reservoir. The drug reservoir contains about 0.1 - 40 wt% of at least one drug, which is selected from the group consisting of fentanyl, oxybutynin, and fluoxetine. (Page 8, line 1 to 21; page 23; FIGs. 1-3)

Claim 24 is directed to a transdermal drug delivery device having a backing layer, a drug reservoir and a means for maintaining the device in drug transmitting relationship with a body surface or membrane. The drug reservoir is on or adjacent the skin-proximal side of the backing layer. The drug reservoir has a melt-blended mixture of at least one drug and a polymer consisting of polyurethane polymer. The polyurethane polymer has a process temperature of less than about 150 °C. The polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in

the drug reservoir. The drug reservoir contains 1 – 10 wt% fentanyl base. (Page 8, line 1 to 21; page 24; page 17, lines 3-4; FIGs. 1-3)

Claim 25 is directed to a transdermal drug delivery device having a backing layer, a drug reservoir and a means for maintaining the device in drug transmitting relationship with a body surface or membrane. The drug reservoir is on or adjacent the skin-proximal side of the backing layer. The drug reservoir has a melt-blended mixture of at least one drug and a polymer consisting of polyurethane polymer. The polyurethane polymer has a process temperature of less than about 150 °C. The polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in the drug reservoir. The drug reservoir contains 1 – 10 wt% fentanyl base and 0 – 20 wt% of a permeation enhancer. (Page 8, line 1 to 21; page 24; page 17, lines 3-4; FIGs. 1-3)

Claim 26 is directed to a transdermal drug delivery device having a backing layer, a drug reservoir and a means for maintaining the device in drug transmitting relationship with a body surface or membrane. The drug reservoir is on or adjacent the skin-proximal side of the backing layer. The drug reservoir has a melt-blended mixture of at least one drug and a polymer consisting of polyurethane polymer. The polyurethane polymer has a process temperature of less than about 150 °C. The polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in the drug reservoir. The drug reservoir contains 1 – 10 wt% fentanyl base and 2 – 15 wt% of a permeation enhancer. (Page 8, line 1 to 21; page 24; page 17, lines 3-4; FIGs. 1-3)

Claim 27 is directed to a transdermal drug delivery device having a backing layer, a drug reservoir and a means for maintaining the device in drug transmitting relationship with a body surface or membrane. The drug reservoir is on or adjacent the skin-proximal side of the backing layer. The drug reservoir has a melt-blended mixture of at least one drug and a polymer consisting of polyurethane polymer. The polyurethane polymer has a process temperature of less than about 150 °C. The polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in the drug reservoir. The drug reservoir contains 4 – 7 wt% fentanyl base, 4 – 13 wt% of a permeation enhancer, and 75 – 92 wt% of a polyether polyurethane. (Page 8, line 1 to 21; page 24; FIGs. 1-3)

Claim 28 is directed to a transdermal drug delivery device having a backing layer, a drug reservoir and a means for maintaining the device in drug transmitting relationship with a body surface or membrane. The drug reservoir is on or adjacent the skin-proximal side of the backing layer. The drug reservoir has a melt-blended mixture of at least one drug and a polymer consisting of polyurethane polymer. The polyurethane polymer has a process temperature of less than about 150 °C. The polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in the drug reservoir. The drug reservoir contains 4 – 7 wt% fentanyl base, 4 – 13 wt% of a permeation enhancer, and 75 – 92 wt% of a polyether polyurethane. The permeation enhancer is selected from monoglycerides and lauryl pyroglutamate. (Page 8, line 1 to 21; page 24; FIGs. 1-3)

Claim 29 is directed to a transdermal drug delivery device of claim 28 and further that the monoglyceride is glycerol monolaurate. (Page 8, line 1 to 21; page 24; FIGs. 1-3)

Claim 30 is directed to a transdermal drug delivery device of claim 28 and further that the wherein the permeation enhancer comprises lauryl pyroglutamate. (Page 8, line 1 to 21; page 24; FIGs. 1-3)

Claim 31 is directed to a transdermal drug delivery device having a backing layer, a drug reservoir and a means for maintaining the device in drug transmitting relationship with a body surface or membrane. The drug reservoir is on or adjacent the skin-proximal side of the backing layer. The drug reservoir has a melt-blended mixture of at least one drug and a polymer consisting of polyurethane polymer. The polyurethane polymer has a process temperature of less than about 150 °C. The polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in the drug reservoir. The means for maintaining the device in drug transmitting relationship with a body surface or membrane comprises an in-line contact adhesive on the skin-proximal surface of the drug reservoir. (Page 8, line 1 to 21; page 24, Fig. 1, Fig. 3)

Claim 32 is directed to a transdermal drug delivery device of claim 31 and further that the adhesive comprises an acrylate adhesive. (Page 8, line 1 to 21; page 25, Fig. 1, Fig. 3, page 12, line 18)

Claim 33 is directed to a transdermal drug delivery device having a backing layer, a drug reservoir and a means for maintaining the device in drug transmitting relationship with a body surface or membrane. The drug reservoir is on or adjacent the skin-proximal side of the backing layer. The drug reservoir has a melt-blended mixture of at least one drug and a polymer consisting of polyurethane polymer. The polyurethane polymer has a process temperature of less than about 150 °C. The polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in the drug reservoir. The mixture has a room-temperature modulus between about 0.1 – 100 MPa. (Page 8, line 1 to 21; page 18, line 18 to page 19, line 4; page 25; page 16, lines 5-6; FIGs. 1-3)

Claim 54 is directed to a transdermal drug delivery device having a backing layer, a drug reservoir and a means for maintaining the device in drug transmitting relationship with a body surface or membrane. The drug reservoir is on or adjacent the skin-proximal side of the backing layer. The drug reservoir has a melt-blended mixture of at least one drug and a polymer consisting of polyurethane polymer. The polyurethane polymer has a process temperature of less than about 150 °C. The polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in the drug reservoir. There is no organic solvent without which the at least one drug cannot be directly melt blended with the polymer at less than about 150 °C and that the reservoir is stable against phase separation of dissolved material. (Page 8, line 1 to 21; page 18, line 18 to page 19, line 4; page 25; page 4, lines 7-12; FIGs. 1-3)

Claim 55 is directed to a transdermal drug delivery device having a backing layer, a drug reservoir and an adhesive for maintaining the device in drug transmitting relationship with a body surface or membrane. The drug reservoir is on or adjacent the skin-proximal side of the backing layer. The drug reservoir has a melt-blended mixture of at least one drug and a polymer consisting of polyurethane polymer. The polyurethane polymer has a process temperature of less than about 150 °C. The polyurethane polymer is a polyether polyurethane and comprises reaction product of at least one aliphatic diisocyanate, polyether polyol and diol such that the polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to

result in the drug reservoir. The polyether polyol is a mixture of at least two polymers selected from the group consisting of polytetramethylene ether glycol, polypropylene glycol, polyethylene glycol, and propylene glycol and wherein the at least one permeation enhancer comprises a fatty acid ester, wherein the reservoir is stable against phase separation of dissolved material. (Page 8, line 1 to 21; page 18, line 18 to page 19, line 4; page 12, lines 1-9; page 23, lines 1-10; page 4, lines 7-12; FIGs. 1-3)

Claim 56 is directed to a transdermal drug delivery device having a backing layer, a drug reservoir and an adhesive for maintaining the device in drug transmitting relationship with a body surface or membrane. The drug reservoir is on or adjacent the skin-proximal side of the backing layer. The drug reservoir has a melt-blended mixture of at least one drug and a polymer consisting of polyurethane polymer. The polyurethane polymer has a process temperature of less than about 150 °C. The polyurethane polymer is a polyether polyurethane and comprises reaction product of at least one aliphatic diisocyanate, polyether polyol and diol such that the polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in the drug reservoir. The reservoir is stable against phase separation of dissolved material. (Page 8, line 1 to 21; page 18, line 18 to page 19, line 4; page 23, lines 1-10; page 4, lines 7-12; FIGs. 1-3)

Claim 57 is directed to a transdermal drug delivery device having a backing layer, a drug reservoir and an adhesive for maintaining the device in drug transmitting relationship with a body surface or membrane. The drug reservoir is on or adjacent the skin-proximal side of the backing layer. The drug reservoir has a melt-blended mixture of at least one drug and a polymer consisting of polyurethane polymer. The polyurethane polymer as 75 wt% to 95 wt% of the drug reservoir and being a polyether polyurethane having a process temperature of less than about 150 °C. The polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in the drug reservoir. The polyurethane polymer can be directly melt blended starting from granules with the at least one drug selected from the group consisting of fentanyl, oxybutynin, and fluoxetine at less than about 150 °C without an organic solvent to result in the drug reservoir. (Page 8, line 1 to 21; page 16, lines 16-19; page 18, line 18 to page 19, line 4; page 23, lines 26-27; FIGs. 1-3)

Claim 59 is directed to a transdermal drug delivery device having a backing layer, a drug reservoir and a means for maintaining the device in drug transmitting relationship with a body surface or membrane. The drug reservoir is on or adjacent the skin-proximal side of the backing layer. The drug reservoir has a melt-blended mixture of at least one drug and a polymer consisting of polyurethane polymer. The polyurethane polymer has a process temperature of less than about 150 °C. The polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in the drug reservoir. The polyurethane polymer constitutes 75 wt% to 95 wt% of the reservoir and the polyurethane polymer can be melt blended starting from granules with the at least one drug. (Page 8, line 1 to 21; page 18, line 18 to page 19, line 4; page 16, lines 16-19; FIGs. 1-3)

Claim 60 is directed to a transdermal drug delivery device having a backing layer, a drug reservoir and a means for maintaining the device in drug transmitting relationship with a body surface or membrane. The drug reservoir is on or adjacent the skin-proximal side of the backing layer. The drug reservoir has a melt-blended mixture of at least one drug and a polymer consisting of polyurethane polymer. The polyurethane polymer has a process temperature of less than about 150 °C. The polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in the drug reservoir. The polyurethane polymer can be melt blended starting from granules with the at least one drug. (Page 8, line 1 to 21; page 18, line 18 to page 19, line 4; FIGs. 1-3)

Grounds of Rejection to be Reviewed on Appeal

Whether claims 12, 13, 15-20, 22, 33, and 54 are anticipated by US4638043 ('043 Szycher) under 35 USC § 102(b). Whether claims 12-20, 22, 33, 54-57 and 59-60 are unpatentable over US4638043 ('043,Szycher) under 35 USC § 103(a). Whether claims 12-33, 54-57 and 59-60 are unpatentable over US4638043 in view of US5273757('757 Jaeger) or vise versa. Whether claims 21, 28, 29, and 32 are unpatentable over US4638043 in view of US5273757('757 Jaeger) and further in view of US6139866 ('866 Chono). Whether claims 21, 28, and 30 are unpatentable over US4638043 in view of

US5273757('757 Jaeger) and further in view of US5066648 ('648 Alexander). Whether claims 32 are unpatentable over US4638043 in view of US5273757('757 Jaeger) and further in view of US5599289 ('289 Castellana) (the Examiner cited US5599648 as prior art but Applicants think the Examiner was actually referring to US5599289 ('289 Castellana) instead of US5599648, which is on printing and is irrelevant to drug delivery).

Argument

The rejected claims do not stand and fall together, as they will be evident in the argument below. The groupings are argued as the follows.

35 USC § 102(b): The claims are not anticipated by US4638043 ('043 Szycher)

Claim 12, 13

Claims 12, 13, 15-20, 22, 23, and 54 under 35 USC 102 were finally rejected as being anticipated by US4638043 ('043 Szycher). Each of the above claims are directed a transdermal drug delivery device having a backing layer, a drug reservoir and a means for maintaining the device in drug transmitting relationship with a body surface or membrane. The drug reservoir is on or adjacent the skin-proximal side of the backing layer. The drug reservoir has a melt-blended mixture of at least one drug and a polymer consisting of polyurethane polymer. The polyurethane polymer has a process temperature of less than about 150 °C. The polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in the drug reservoir.

In the Final Office Action, the Examiner cited Szycher and asserted that the process temperature of polyurethane is inherent and that mixing the drug in the polyurethane layer before or after the curing is directed to method of product and does not impart patentability to the claims directed to product. The Examiner asserted that the end product is not materially different from the product of the prior art and that the reference (Szycher) disclosed the polyurethane made from the same elements as instantly claimed.

Applicants submit that (1) the process temperature is not inherent, (2) the melt-mixing of the drug in polyurethane without curing does impart patentability to the

product claims; and (3) the end product is materially different from the product of Szycher.

Regarding Szycher, he described only about UNCURED material as far as mixing or blending is concerned. He never mentioned that the cured material can be mixed or blended, regardless of temperature. He never mentioned that the polyurethane layer is liquid at room temperature, only that the precured oligomeric material is liquid (which before curing is not suitable for a matrix layer in the device because as a liquid it would flow). It is submitted that Szycher mixed PRECURED oligomeric liquid at room temperature (see column 2, lines 42-47) to be polymerized by curing, not the polymerized polymer. The liquid PRECURED polymeric liquid is not yet cured and therefore is not polyurethane. Szycher stated clearly that the drug dispensing member is comprised of "a polyurethane formed from an oligomer which is cured by actinic radiation....", the drug is incorporated in the material before the material is cured (Column 4, lines 10-14). The polyurethane is ***formed from an oligomer by curing***. Curing changes the thermal and mechanical property of a material, because of cross-linking formed in the curing reaction.

(1) the process temperature is not inherent

First, about process temperature, as Applicants have pointed out in the response filed January 17, 2006 (see top of page 9 of said response), melt-blending involves melting something solid to form a melt and blending a drug in the melt. On pages 3-4 of our specification we mentioned hot melt adhesive, process temperature and polyurethane. As the term "melt-blend" or "melt mix" indicates, melting is involved. The word "melt" is a feature in the claim and cannot simply be disregarded. The conventional use of terms like hot melt adhesive, process temperature and mixing in hot melt technology is clear that a polymer for containing polymer is melted to mix in a drug. E.g., US5662923 ('923 Roreger) (which was cited in earlier 7/19/2005 office action) discussed "hot-melt adhesive" and "melting" (e.g., col 2, lines 62-64); "melting", "homogenizing", "mixing" (e.g., col. 3, line 61-62; col 8, lines 19-20); and "processing temperature" (e.g., col. 5, lines 63-65). As another example, melting thermoplastic polymer and blending in the drug are also described in described in US6010715. Thus, it is clear that to those skilled in the art, reading the present specification as a whole, that melt blending or melt mixing

in the present invention involves raising the temperature to melt the polyurethane from a unmelted state and mixing in the drug (as we do in our Example 1 in melting granules and mixing in a drug). Such melt-blending usually is done with an extruder or some kind of a blender or mixer with a heater. After melt-blending and cooling the melt-blended material to a temperature at which the product can be used, the material become unmelted, usually as a solid phase material which can again be remelted by increasing temperature. It is clear that that what we refer to as "process temperature" of the polyurethane polymer is the temperature at which the ***polyurethane*** polymer can be ***melted and blended*** with drug.

Szycher never mentioned melt blending. In fact, the word "melt" never appeared in the patent. Further, the only times Szycher talked about heat were on curing or that drugs were heat labile. Nothing was ever said about melting. Szycher '043 has nothing to do with melt blending polymer and drug.

Melt-blendability is a property of the polyurethane in the claimed device. In the presently claimed invention, the polyurethane polymer can be directly ***melt blended*** with the at least one drug at less than about 150 °C without an organic solvent. The polyurethane in the device must be able to be processed by melt-blending. There is no indication that the material described by Szycher can be processed in melt-blending.

In fact, Applicants submit that the precured liquid material of Szycher cannot be melt-blended, since it being already a liquid cannot be processed by melting. Just because something can be mixed in room temperature does not mean it can be melt-blended. By analogy, concrete mix before setting can be mixed in room temperature. That does not mean the concrete mix can be melt-blended. Second, there is no indication that after curing or cross-linking the cured polymers can be melt-blended at all. UV curing or cross-linking is a generally irreversible chemical reaction. Once cured, the material cannot be uncured, at least not by simple heating or cooling processes. Thus, there is no indication that the polyurethane in the UV-cured material can be melt-blended anymore, much less be processed at a temperature of less than about 150 °C without an organic solvent. There is no indication that the material described by Szycher can be processed in melt-blending. Szycher might have mentioned raising temperature to cause the curing of oligomers, but such curing temperature is certainly not the "processing

temperature" in which the polyurethane material is heated to melt in melt-blending. There never is any melting in Szycher. Thus, the melting temperature of the present invention is not inherent in Szycher.

The Examiner tried to argue that Szycher described a melt-blending process by alleging that since the Szycher's oligomer material is liquid in room temperature it can be heated to melt a drug into the liquid. This logic is flawed. First, the uncured oligomer would not be considered a melt-blendable polyurethane. Even Szycher called it "oligomer" before curing and "cured polyurethane" after curing. Second, the oligomer was liquid and was not meltable. One would no more likely to say that this liquid oligomer is meltable than "liquid water is meltable" or "gaseous oxygen is meltable." Third, Szycher never mentioned melting a drug either. Szycher never mentioned "melt" or "melting", period. The Examiner must not read the reference out of context and add her own new matter into the reference. There is nothing inherent about heating to melt a drug about Szycher. Some drugs degrade quickly when heated. Some drugs simply cannot be melted. Even if assuming Szycher had mentioned melting a drug, melting a drug has nothing to do with a polyurethane polymer that is melt-blendable (i.e., polyurethane that can be melted and blended).

(2) Mixing of drug in polyurethane before or after curing imparts patentability

We submit the melt mixing of the drug in polyurethane without the need for curing does impart patentability to the product claims. Whether something is cured or not has great impact on the property of a device and thus impact patentability. For analogy, doesn't the claim "a tire made of uncured rubber" have patentability over references that all talk about tires made of cured rubber? By requiring curing, the referenced Szycher material has property vastly different from material that can be melt blended, and therefore cannot be used for anticipating the present invention. The precured oligomer material cannot be melt-blended because it cannot melt. The post-cured polymer cannot be melt-blended because there is no indication that it can melt, and definitely there is no word that it can melt at less than about 150 °C.

(3) The end products are materially different before and after curing

Third, our end product is materially different from the end product of Szycher. In certain claims, the transdermal drug delivery device has a drug reservoir comprising a melt-blended mixture of at least one drug and a polymer consisting of polyurethane polymer, in which the polyurethane polymer has a process temperature of less than about 150 °C, wherein the polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in the drug reservoir. Thus, in our ***end product***, the mixture includes a polyurethane that has a process temperature of less than about 150 °C, at which melt blending can be done. There is absolutely no evidence that the Szycher ***cured*** end product has polyurethane that has such property. There is no evidence at all about a temperature at which the polyurethane in the Szycher ***cured end product*** can become fluid by heating to be blendable, let alone at less than about 150 °C.

(4) Szycher did not show TECOFLEX can be used for drug containing layer

In an effort to allege that Szycher described using TECOFLEX for both the drug containing layer, the Examiner asserted Szycher on col 8, lines 56-65 disclosed drug containing layer made of a reaction product which is TECOFLEX. However, col 8, lines 56-65 is about the substrate, not the drug containing layer. Applicants in an earlier response have already pointed out before that Szycher described TECOFLEX only related to substrate. However, in the Final Rejection, the Examiner further alleged that Szycher on col 6, lines 20-23 "disclosed that the materials used to make the drug containing layers is the same as the materials used to make the substrate but without the drug" and that "therefore, TECOFLEX can be used for both the drug containing layer and the substrate." Applicants submit that is not the case at all, but rather this passage is still about the substrate. First, Szycher DID NOT "disclosed that the materials used to make the drug containing layers is the same as the materials used to make the substrate but without the drug". Rather, Szycher merely said that "the polyurethane formed in the drug release system" is also suitable for the substrate layer. Szycher in the sections just before the cited col 6, lines 20-23 was actually describing the making of the substrate 12. Then on col 6, line 17-20 Szycher said, "Also suitable for use is the polyurethane formed in the drug release system described above and set forth in U.S. Pat. No. 4,483,759 to

Michael Azycher et al.", meaning that the drug layer material can also be used for the substrate.

Thus, clearly, Szycher did NOT disclose "the materials used to make the drug containing layers is the same as the materials used to make the substrate but without the drug" but rather that the material of the drug layer can be used for the substrate. This is a critical difference. Any student of logics knows that "A can be used for B" does not mean "B can be used for A" and definitely does not mean "A is the same as B." The requirement for the material for the drug containing layer is much more restrictive than the requirement for the substrate. The polymer for the drug-containing layer being applicable for making the substrate does not mean the substrate material can be used for the drug-containing layer. Thus, Szycher did not teach that TECOFLEX (which is usable as substrate) can be used for the drug-containing layer at all.

Even if, arguando, assuming the Szycher did suggest TECOFLEX could be used in the drug-containing layer (and Applicants do not agree he did), that still does not mean Szycher suggested TECOFLEX of the kind having processing temperature of less than about 150 °C was to be used, or that it could be used without curing. TECOFLEX is brand name, which emcompassed a host of products of various melting temperatures. There certainly is no indication or suggestion on processing temperature of less than about 150 °C.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently as described, in a single reference. Verdegaal Bros. v Union Oil., 814 F2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir.), cert. denied, 484 U.S. 827 (1987). It is submitted that the Examiner has failed to show that all elements in the claims are found in the referenced Szycher patent.

Certain claims are separately patentable and further different from Szycher

Applicant submit that other than claims 13-14 which are related to process temperatures, the other claims under appeal do not stand and fall with claim 12, and are patentable separately. The reason is that the monomeric composition of the polyurethane, the permeation enhancers, and specific drug were mentioned and these would affect the process temperature of the mixture and the amount of the drug as

delivered, as well as the adhesive property of the resulting material. Something that can be used in one system does not mean it will be applicable in a different system. Claim 15 to 19 mention specifics about the polyurethane. Claims 20-32, 57, and 59 include specific ranges of drug, permeation enhancer, or polyurethane in the drug reservoir. Claims 27-32, 57, and 59 especially stated the amount of polyurethane polymer in the drug reservoir. Claims 31-32 address having an in-line adhesive. Claim 33 addresses the mixture having a particular modulus. Claims 54-56 mentions not having phase separation. These claims are not anticipated by Szycher.

35 USC § 103(a) Patentability

The claims are patentable over US4638043 ('043 Szycher)

Claim 12-14

The Examiner rejected claims 12-20, 22, 33, 54 and 58-61under 35 USC 103 as being unpatentable over US4638043 ('043,Szycher). The Examiner asserted that "043 discloses a transdermal drug releasing patch that comprises support layer (i.e., backing layer), polymer layer of polyurethane containing a drug and a pressure sensitive adhesive layer and that the drug is contained in an amount of 1-10% in the polyurethane layer and includes analgesic. The Examiner further asserted (citing Szycher col 8, lines 56-65) that the polyurethane comprises reaction products of dicyclohexyl methane diisocyanate, polytetramethylene ether polyol and 1,4-butane diol.

Applicants have already submitted that Szycher col 8, lines 56-65 is about the substrate, not about the drug-containing layer. Regarding dicyclohexyl methane diisocyanate, polytetramethylene ether polyol and 1,4-butane diol, it is noted that these are also mentioned in col 5, lines 39-43, which is also the description on material for the substrate, not the drug containing material.

The Examiner repeated the assertion that the reference '043 "suggested that both drug containing layer and the substrate layer can be made from the same polyurethane (citing col 6, lines 20-23). Again, this is based on the flawed logic that if the material of A can be used for B, then the material for B can be used for making A. Szycher only suggested that the material for making the drug releasing member can be used for making

the substrate, but said nothing about the reverse. Even if, arguando, assuming he did disclose that material for the drug layer, that material is not a melt-blendable polyurethane, as Applicant have submitted above in the section on 35 USC § 102(b) anticipation.

The Examiner admitted that '043 does not explicitly teach that the process temperature and the modulus of the polyurethane polymer, but she asserted that process temperature and the modulus of the polyurethane polymer disclosed by US'043 are expected to be the same as what is claimed in the instant application because the reference teaches the same polymer formed from the same polymer reaction that is liquid at room temperature and that it would be obvious to provide "polyurethane polymer layer containing a drug wherein the polyurethane layer is liquid at room temperature" and "adjust the temperature to the required to melt the drug into the liquid polyurethane polymer according to specific drug used without the use of any solvents, motivated by the teaching of US '043...."

Applicants have shown above that melt-blending has never been suggested by '043 Szycher. Applicants have also already submitted that Szycher never mentioned melting at all in the whole patent. Nothing was even said by Szycher that anything is meltable or melt-blendable at about 150 °C without an organic solvent. How then can Szycher give any motivation to melt-blending a polymer with a drug at less than about 150 °C without an organic solvent? How can there be any suggestion of melt-blending if no melting is mentioned and all Azycher talked about was curing? If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims prima facie obvious. In re Ratti, 270 F.2d 810, 123 USPQ 349 (CCPA 1959). The ***principle of the prior art Azycher reference was curing*** a oligomer liquid to make a solid film. Applicants fail to see how Szycher, which focused on curing to form a polyurethane polymer, can be modified to become the present invention, let alone doing so without changing the principle of Schyer's invention.

Certain claims are separately patentable and further different from Szycher

Applicant submit that other than claims 13-14, which are related to process temperatures, the other claims under appeal do not stand and fall with claim 12. The reason is that the monomeric composition of the polyurethane, the permeation enhancers, and the specific drug affect the process temperature of the mixture and the amount of the drug as delivered, as well as the adhesive property of the resulting material. Something that can be used in one system does not mean it will be applicable in a different system. Claim 15 to 19 mention specifics about the polyurethane. Claims 20-32, 57, and 59 include specific ranges of drug, permeation enhancer, or polyurethane in the drug reservoir. Claims 27-32, 57, and 59 especially stated the amount of polyurethane polymer in the drug reservoir. Claims 31-32 address having an in-line adhesive. Claim 33 addresses the mixture having a particular modulus. Claims 54-56 mentions not having phase separation. These claims are neither anticipated or rendered obvious by Szycher.

The claims are patentable over US4638043 in view of US5273757('757 Jaeger) or vise versa

Claim 12-14

The Examiner rejected claims 12-33, 54-61 under 35 USC 103 as being unpatentable over US4638043 in view of US5273757('757 Jaeger) or vise versa. The Examiner asserted that specific drugs, permeation enhancers and acrylate adhesive do not impart patentability to the claims and that it would be obvious for one skilled in the art to further follow the teaching of '757 Jaeger about hot melt adhesive layer comprising 10-100% polyurethane adhesive, 10-80% plasticizer such as fatty acid esters, and drug such as fentanyl using temperature between 40°C to 80°C without solvent.

Applicants submit that US4638043 is irrelevant as discussed above and Jaeger does not cure the shortcomings of '043Szycher.

Regarding Jaeger, Jaeger stated that "The invention relates to an apparatus for the release of substances from hot melt pressure sensitive adhesives, with a non-uniform or irregular distribution of the substances... ." (col 1, lines 15-18) and "According to the invention this problem is solved by an apparatus for the release of active substances from hot melt pressure sensitive adhesives with a non-uniform or regular distribution of the

substances" (col 2, lines 46-50). It is not clear whether Jaeger meant that all of the formulations were irregular and nonuniform or that some were irregular and nonuniform and some were not. One thing for sure, at least some (and likely all) of his formulations were nonuniform and irregular. An important difference about '757 is that it teaches that the "pressure sensitive adhesive can contain only up to 10 to 50% by weight of polyurethane" (see column 6, lines 12-13). There are a lot of other material in the adhesive, such as 10-80% hydrogenated alcohol, 10-80% hydrocarbon resin, 1 to 40% of esters of vegetable fatty acids, and possible additionally up to 5% antiagers, and up to 70% fillers. Much of these other ingredients were soft materials and perhaps liquid, including a large amount of plasticizers. There may be as low as 10% polyurethane polymer with as much as 40% vegetable fatty acids ester plasticizer. With "nonuniform and irregular" distribution of substances, the resultant material may be like peanut butter with polymer particles mixed in a semiliquid form. Jaeger did not give any indication that it was not so, or at least what formulations were not so. Polyurethane was only one of many scores of alternative polymers listed. Perhaps Jaeger's polyurethane products were like peanut butter and ethylcellulose product were not. Jaeger did not differentiate among them. How is a reader skilled in art to know which would make a uniform product.

Further, different drugs and ingredients affect the temperature tolerance as well as the physical property of the drug-containing layer. As mentioned above, there are a lot of other materials in the Jaeger adhesive: hydrogenated alcohol, hydrocarbon resin, esters of vegetable fatty acids, antiagers, and fillers. Esters of vegetable fatty acids, hydrogenated alcohol, and hydrocarbon resin have plasticizer functions. It is a scientific fact that plasticizers are able to decrease the glass transition temperature and the melt viscosity of a hot melt polymer. "With the addition of a plasticizer, a hot melt process can be conducted with lower temperature and with less torque." (quoted from (paragraph 2 on page 2) "The Role of Plasticizers as Functional Excipients in Pharmaceutical Dosage Forms Prepared by Hot-Melt Extrusion", Pharmaceutical Coating Bulletin 102-6, Morflex Inc. 2004, said reference is quoted for scientific facts, not for prior art purpose). See also a statement in earlier publication US 5662923 (Roreger), col 3, lines 1-2 about pressure sensitive hot melt adhesive: "The softening temperature is reduced by so called

plasticizers...." With a large amount of such non-polyurethane plasticizers in the Jaeger adhesive, the thermal property of the adhesive is very different from that of the polyurethane ingredient. There is no indication what the melt-blending processing temperature of the polyurethane in the adhesive is. Jaeger only stated that the pressure sensitive adhesive (i.e., the adhesive mixture with drug active substance as well as other exipients since it can release the active substance) has a processing temperature of 40 – 80 °C (see e.g., column 2 lines 50-51). But Jaeger ***did not say that the polyurethane of the adhesive has a processing temperature*** of 40 – 80 °C. There is a difference between the adhesive and its polyurethane ingredient, they are not one and the same. There is no indication that the polyurethane used by Jaeger has a processing temperature of 40 – 80 °C.

Importantly, there is no working example by Jaeger. Thus, a person will not know what range within the section of description of col. 6, line 12 to 21 related to polyurethane is workable, whether all of the formulations would be like peanut butter or which ranges would not be like peanut butter. Surely not everything, but rather only certain limited ranges, of combinations of the parameters disclosed in that section would be workable for a uniform product, if at all, since the ranges were so large (e.g., fillers up to 70%, hydrogenated oil 10 to 80%, hydrocarbon resin 10 to 80%, esters of vegetable fatty acids 1 to 40%, up to 5 % antiagers). How is a person skilled in the art to know which combinations of ranges of parameters would work?

Obviousness requires a reasonable expectation of success. See, In re O'Farrell 853 F.2d 894 903-4, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988). Even if a person were foodhardy enough to want to try, there is not expectation of success that polyurethane without a large amount of plasticizer can be processed at that temperature range. Thus, even if assuming one would want the advantages of lower temperature processing and fentanyl and enhancers, one would not glean from Jaeger of melt mixing polyurethance that the polyurethane itself has a low melt-blending processing temperature to make a product.

If a person were to combine Szycher with Jaeger, what would the result be, cured polyurethane with lots of plasticizers? Howabout vise versa, uncured oligomers with lots

of plasticizers? Such combinations would not result in the claimed product of the present application.

It is not obvious at all that the polyurethane with processing temperature of less than 150°C is present in the adhesive in Jaeger or that Jaeger could produce uniform hot melt drug-containing layer from polyurethane. Thus, no combination of Szycher and Jaeger in whatever way, or vice versa will render the present invention obvious.

Other claims patentable separately

Regarding claims other than claim 12, and 13-14 which are related to process temperatures, the other claims under appeal do not stand and fall with claim 12. The reason is that the monomeric composition of the polyurethane, the permeation enhancers, and the specific drug affect the process temperature of the mixture and the amount of the drug as delivered. In particular, claim 15 to 19 mention specifics about the polyurethane. Claims 20-32, 57, and 59 include specific ranges of drug, permeation enhancer, or polyurethane in the drug reservoir. These ranges are generally outside the ranges of what Jaeger disclosed. Claims 27-32, 57, and 59 especially stated the amount of polyurethane polymer in the drug reservoir and the ranges are substantially more than that disclosed by Jaeger. Claims 31-32 address having an in-line adhesive. Claim 33 addresses the mixture having a particular modulus. Claims 54-56 mentions not having phase separation. No combination of Szycher and Jaeger would render these claims obvious.

The claims are patentable over US4638043 in view of US5273757('757 Jaeger) and further in view of US6139866 ('866 Chono).

Claims 21, 28-29

The Examiner rejected claims 21, 28, 29, and 32 under 35 USC 103 as being unpatentable over US4638043 in view of US5273757('757 Jaeger) and further in view of US6139866 ('866 Chono). The Examiner asserted that because '866 Chono teaches delivery fentanyl in a formulation with 0.05% fentqanyl, 0.1-98% of pressure sensibive adhesive that can be acrylate adhesive, and 0.01-20% of permeation enhancer such as glycerol such as glycerol monolaurate it would be obvious to combine with '43 Szycher and '757 jaeger to arrive at the present invention.

The irrelevance of US4638043 and US5273757 have been discussed above. Chono did not cure the shortcomings of '043 and '757. The Examiner asserted that Chono disclosed formulations comprising fentanyl, acrylate adhesive, and permeation enhancers such as glycerol monolaurate and thus a skilled person would be motivated to use glycerol monolaurate and use acrylate as skin contact adhesive. However, it is noted that Chono did not mention polyurethane for the drug layer at all. Where Chono mentioned polyurethane, he only refered to the backing layer (column 5, line 43-44). Thus, Chono ***never intended polyurethane*** to be used in the drug layer, but only for the backing layer. Further, even for those adhesives (polyurethane was not mentioned), the adhesive/drug mixing was apparently done ***with solvent*** (column 5, lines 24-35 mentioning solvent method; column 6, lines 16-20 mentioning solvent ethanol). Thus, although the Chono patent discloses fentanyl and certain permeation enhancers, it certainly is irrelevant for melt-blending with drug at a low temperature using a polyurethane polymer that can be processed at or below 150 °C. Chono apparently thought of polyurethane as unsuitable for holding the drug and enhancers but only suitable for backing.

Furthermore, an enhancer or drug that works for one drug reservoir may not work for another drug reservoir with a different polymer, considering there are vast differences in solubility, permeation, and effect on adhesiveness, etc. Even if one were assumed to want to combine Chono with the other references, one would only use enhancers for non-polyurethane reservoir and only use polyurethane for the backing.

The Examiner asserted that there is reasonable expectation of having a transdermal melt blend matrix comprising polyurethane, fentanyl and glycerol monolaurate and acrylate adhesive skin contact layer. Applicants submit that Chono, suggesting using solvent for putting drug into an adhesive and never having mentioned polyurethane as usable for containing a drug, would provide no expectation of success at all. Thus, even if claim 12 falls, the other claims that mention the specifics of polyurethane components, fentanyl, glycerol monolaurate, or acrylate adhesive skin contact layer would still stand.

Other claims patentable separately

Applicants submit that claims 31-32 address having an in-line adhesive and therefore are separately patentable from the other claims (21, 28-29) rejected under references including Chono. No combination of Szycher, Jaeger and Chono would render these claims obvious.

The claims are patentable over US4638043 in view of US5273757('757 Jaeger) and further in view of US5066648 ('648 Alexander)

Claims 21, 28, and 30

Claims 21, 28, and 30 are rejected under 35 USC 103 (a) as being unpatentable over US4638043 in view of US5273757('757 Jaeger) and further in view of US5066648 ('648 Alexander).

The irrelevance of US4638043 and US5273757 has been discussed above. Alexander does not cure the shortcomings of '043 and '757. The Examiner asserted that Alexander teaches pyroglutamic acid esters as permeation enhancers for analgesics and sedatives, and therefore one skilled in the art will be led to deliver fentanyl with the enhancers in our claimed invention. However, surely the Examiner is not saying that all analgesics and sedatives can be delivered with the aid of a particular permeation enhancer and that just because a permeation enhancer works with one analgesic it would work with all other analgesics. Anybody skilled in the art knows that permeation enhancers do not function the same way for different drugs in different matrixes. An enhancer that works for drug A may not work for drug B in the same polymer. Further, an enhancer that works in a polymeric matrix may not work in another polymeric matrix. Alexander does ***not mention fentanyl***, and does ***not mention polyurethane*** as the drug layer carrier polymer. Furthermore, Alexander has ***nothing to do with melt-blending***. Even if it is assumed that one would combine the references there is no expectation of success that fentanyl can be effectively delivered in a polyurethane melt blended mix. Thus, a person skilled in the art will not look to Alexander for suggestions on melt-blending of fentanyl in polyurethane at all. Even if one is assumed for argument's sake to look for guidance at Alexander, there is no expectation of success.

Claims 21, 28, and 30 stand and fall together.

The claims are patentable over US4638043 in view of US5273757('757 Jaeger) and further in view of US5599289 ('289 Castellana)

The Examiner rejected claims 32 under 35 USC 103(a) as being unpatentable over US4638043 in view of US5273757('757 Jaeger) and further in view of US5599648 (however, Applicants think the Examiner was actually referring to US5599289 ('289 Castellana)) instead, since is US5599648 is on printing and is irrelevant to drug delivery.

The irrelevance of US4638043 and US5273757 has been discussed above. Castellana does not cure the shortcomings of '043 and '757.

First, Castellana, being on a wound dressing, is not analogous art. The Examiner asserted because Castellana'289 is on the field of Applicants' endeavor it is relevant. However, transdermal drug delivery systems are dynamic systems that require drug flux from the patch and a polymer that the drug either is stored in or must traverse through necessarily must possess certain drug solubility, permeation and adhesive property to work. Unlike in a wound dressing, drug is continually leaving the drug reservoir in application. What can be used in a simple wound dressing, even one with some antibiotic to prevent infection, does not translate into applicability in a transdermal system.

Second, Castellana taught only one polymer layer. He did not teach or suggest having an ***inline contact adhesive on the skin-proximal surface of the drug reservoir*** (which contains polyurethane). The Examiner asserted that Castellana teaches wound dressing comprising skin contact acrylate adhesive layer and therefore one would make the presently claimed invention. However, There is no description by Castellana that another polymer is used as an in-line adhesive on a drug reservoir having a ***different polymer***, much less having an acrylate adhesive on a polyurethane reservoir. Thus, the use of acrylate adhesive by Castellana is entirely different from what is claimed in claim 32 (which depends from claim 31). For transdermal delivery, even an adhesvie polymer to be used as a drug reservoir by itself may not be suitable for use to be placed on another reservoir drug layer that has a different polymer. In this claimed structure, the drug has to pass from the polyurethane reservoir into the acrylate adhesive before reaching the skin. Castellana does not teach that and there is no expectation of success from Castellana even if one were assumed to want to try. For example, depending on the layers, the solubility of the skin contacting adhesive for the drug may be so high that the

concentration of the drug in that skin contacting adhesive may not be high enough to produce an effective flux. And Castellana has no mention of fentanyl. Thus, who knows what fentanyl will do in the two polymer layers, considering the unpredictability of the combination of two different polymer layers through which fentanyl must migrate? An adhesive that works for one drug may not be effective for transdermal delivery for another drug. And Castellana is not even related to transdermal delivery. How can there be any expectation of success if one were to follow Castellana?

Furthermore, there is no mention of melt mixing temperature and thus Castellana is far removed from the presently claimed invention. Thus, even if with the assumption that some one would want to combine the references as asserted by the Examiner, there is no expectation of success. Without using the present disclosure as a guide, one would not have any expectation of success. However, one cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention. See, In re Fine, 837 F.2d 1071, 1075, 5 USPQ2d 1596 (Fed.Cir.1988).

Conclusion

In view of the foregoing, the claims of the application are not anticipated under 35 U.S.C. § 102(b) and not obvious under 35 U.S.C. § 103(a) over the cited references. Applicants invite the Appeal Board or the Examiner to contact the undersigned at (650) 564-7054 to clarify any unresolved issues raised by this response.

The Commissioner is hereby authorized to charge any additional fees associated with this paper or during the pendency of this application, or credit any overpayment, to Deposit Account No. 10-0750.

Respectfully submitted,

Date: March 15, 2007

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Claims Appendix

1. - 11. (Canceled)

12. A transdermal drug delivery device comprising:

(a) a backing layer;

(b) a drug reservoir on or adjacent the skin-proximal side of the backing layer, said drug reservoir comprising a melt-blended mixture of at least one drug and a polymer consisting of polyurethane polymer, said polyurethane polymer having a process temperature of less than about 150 °C, wherein the polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in the drug reservoir; and

(c) means for maintaining the device in drug transmitting relationship with a body surface or membrane.

13. The device of claim 12 wherein said polyurethane polymer has a process temperature of less than about 100 °C.

14. The device of claim 12 wherein said polyurethane polymer has a process temperature of about 40 – 90 °C.

15. The device of claim 12 wherein said polyurethane polymer is a polyether polyurethane.

16. The device of claim 15 wherein the polyurethane polymer comprises the reaction product of at least one aliphatic diisocyanate, at least one high molecular weight polyether polyol, and at least one low molecular weight glycol.

17. The device of claim 16 wherein the diisocyanate comprises methylene bis(cyclohexyl) diisocyanate, the polyether polyol is selected from the group consisting of poly tetramethylene glycol, poly propylene glycol, and polyethylene glycol.

18. The device of claim 17 wherein the low molecular weight glycol is 1,4-butane diol.

19. The device of claim 17 wherein the polyether polyol is a mixture of at least two polymers selected from the group consisting of polytetramethylene ether glycol, polypropylene glycol, polyethylene glycol, and propylene glycol.

20. The device of claim 12 wherein the drug reservoir contains 0 - 20 wt% of at least one permeation enhancer.

21. The device of claim 20 wherein the permeation enhancer is selected from the group consisting of monoglycerides and lauryl pyroglutamate.

22. The device of claim 12 wherein the drug reservoir contains about 0.1 - 40 wt% of at least one drug.

23. The device of claim 22 wherein the drug is selected from the group consisting of fentanyl, oxybutynin, and fluoxetine.

24. The device of claim 12 wherein the drug reservoir contains 1 – 10 wt% fentanyl base.

25. The device of claim 24 wherein the drug reservoir contains 0 – 20 wt% of a permeation enhancer.

26. The device of claim 24 wherein the drug reservoir contains 2 – 15 wt% of a permeation enhancer.

27. The device of claim 12 wherein the drug reservoir contains 4 – 7 wt% fentanyl base, 4 – 13 wt% of a permeation enhancer, and 75 – 92 wt% of a polyether polyurethane.

28. The device of claim 27 wherein the permeation enhancer is selected from monoglycerides and lauryl pyroglutamate.

29. The device of claim 28 wherein the monoglyceride is glycerol monolaurate.

30. The device of claim 28 wherein the permeation enhancer comprises lauryl pyroglutamate.

31. The device of claim 27 wherein the means for maintaining the device in drug transmitting relationship with a body surface or membrane comprises an in-line contact adhesive on the skin-proximal surface of the drug reservoir.

32. The device of claim 31 wherein the adhesive comprises an acrylate adhesive.

33. The device of claim 12 wherein the mixture has a room-temperature modulus between about 0.1 – 100 MPa.

34. - 53. (Canceled)

54. The device of claim 12 wherein there is no organic solvent without which the at least one drug cannot be directly melt blended with the polymer at less than about 150 °C and that the reservoir is stable against phase separation of dissolved material.

55. A transdermal drug delivery device comprising:

(a) a backing layer;

(b) a drug reservoir on or adjacent the skin-proximal side of the backing layer, said drug reservoir comprising a melt-blended mixture of at least one drug, at least one permeation enhancer and a polymer consisting of polyurethane polymer, said

polyurethane polymer having a process temperature of less than about 150 °C, wherein the polyurethane polymer is a polyether polyurethane and comprises reaction product of at least one aliphatic diisocyanate, polyether polyol and diol such that the polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in the drug reservoir, the polyether polyol is a mixture of at least two polymers selected from the group consisting of polytetramethylene ether glycol, polypropylene glycol, polyethylene glycol, and propylene glycol and wherein the at least one permeation enhancer comprises a fatty acid ester, wherein the reservoir is stable against phase separation of dissolved material; and

(c) adhesive for maintaining the device in drug transmitting relationship with a body surface or membrane.

56. A transdermal drug delivery device comprising:

(a) a backing layer;

(b) a drug reservoir on or adjacent the skin-proximal side of the backing layer, said drug reservoir comprising a melt-blended mixture of at least one drug and a polymer consisting of a polyurethane polymer, said polyurethane polymer having a process temperature of less than about 150 °C, wherein the polyurethane polymer is polyether polyurethane and comprises reaction product of at least one aliphatic diisocyanate, at least one polyether polyol and diol such that the polyurethane polymer can be directly melt blended with the at least one drug at less than about 150 °C without an organic solvent to result in the drug reservoir, wherein the reservoir is stable against phase separation of dissolved material; and

(c) adhesive for maintaining the device in drug transmitting relationship with a body surface or membrane.

57. A transdermal drug delivery device comprising:

(a) a backing layer;

(b) a drug reservoir on or adjacent the skin-proximal side of the backing layer, said drug reservoir comprising a melt-blended mixture of at least one drug and a polymer consisting of a polyurethane polymer , said polyurethane polymer as 75 wt% to 95 wt% of the drug reservoir and being a polyether polyurethane having a process temperature of less than about 150 °C, wherein the polyurethane polymer can be directly melt blended starting from granules with the at least one drug selected from the group consisting of fentanyl, oxybutynin, and fluoxetine at less than about 150 °C without an organic solvent to result in the drug reservoir; and

(c) adhesive for maintaining the device in drug transmitting relationship with a body surface or membrane.

58. (Canceled)

59. The device of claim 12 wherein the polyurethane polymer constitutes 75 wt% to 95 wt% of the reservoir and the polyurethane polymer can be melt blended starting from granules with the at least one drug.

60. The device of claim 12 wherein the polyurethane polymer can be melt blended starting from granules with the at least one drug.

61. (Canceled)

Evidence Appendix

US4638043 ('043 Szycher) cited in 10/20/2006 final office action.

US5273757 ('757 Jaeger) cited in 10/20/2006 final office action.

US6139866 ('866 Chono) cited in 10/20/2006 final office action.

US5066648 ('648 Alexander) cited in 10/20/2006 final office action.

US5599289 ('289 Castellana) cited in 10/20/2006 final office action.*

*(the Examiner cited US5599648 as prior art but Applicants think the Examiner was actually referring to US5599289 ('289 Castellana).

US5662923('923 Roreger) cited in 7/19/2005 office action.

"The Role of Plasticizers as Functional Excipients in Pharmaceutical Dosage Forms Prepared by Hot-Melt Extrusion", Pharmaceutical Coating Bulletin 102-6, Morflex Inc. 2004, cited in the response Applicants filed in December 19, 2006.

Related Proceedings Appendix

None.